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EXAMINER	
KUBELIK, ANNE R	

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1638	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/782,096	CAROZZI ET AL.	
	Examiner	Art Unit	
	Anne R. Kubelik	1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *31 July 2008 and 17 March 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-11,19 and 22-26* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-11,19 and 22-26* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *18 September 2007* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 1-11, 19 and 22-26 are pending.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejections - 35 USC § 112

3. Claims 1-11, 19 and 22-26 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for nucleic acids encoding coleopteran, lepidopteran or heteropteran toxins with 95% identity to SEQ ID NO:2, 4 and 6, host cells, plants, plant cells and seeds comprising them, and method of using them to make SEQ ID NO:2, 4 or 6, does not reasonably provide enablement for nucleic acids encoding such toxins with 90% identity to SEQ ID NO:2, 4 and 6, or nucleic acids with 90 or 95% identity to SEQ ID NO:1, 3 or 5, host cells, plants, plant cells and seeds comprising them, and method of using them to make a pesticidal protein. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The rejection is modified from the rejection set forth in the Office action mailed 20 May 2008, as applied to claims 1-11, 19 and 22-23. Applicant's arguments filed 31 July 2008 have been fully considered but they are not persuasive.

The claims are broadly drawn to nucleic acids encoding a pesticidal protein with 90% identity to SEQ ID NO:2, 4 or 6, nucleic acids with 90% identity to SEQ ID NO:1, 3 or 5, or a complement of those nucleic acids, host cells, plants, plant cells and seeds comprising them, and

method of using them to make a pesticidal protein with 90% identity to SEQ ID NO:2, 4 or 6 and a pesticidal protein encoded by a nucleic acid with 90% identity to SEQ ID NO:1, 3 or 5.

The instant specification, however, only discusses sequencing of DNAs from non-publicly available bacterial strain ATX13026 (examples 1-4), identification of a nucleic acid, SEQ ID NO:1, that encodes a protein, SEQ ID NO:2, with 28% identity to the delta endotoxin cry8Aa, and an alternate start site variants, SEQ ID NO:4, which encode SEQ ID NOs:4 and 6, respectively (examples 5-6); assay of the protein for pesticidal activity against a number of pests, including the Coleopterans *D. virgifera virgifera* and *D. undecimpunctata*, the Heteropteran *T. ni*, and the Lepidopteran *L. lineolaris* (examples 7-12), and prophetic guidance for expression in plants (examples 13-15).

The instant specification fails to provide guidance for how to make the full scope of nucleic acids encoding pesticidal protein with 90% identity to SEQ ID NO:2, 4 or 6 or the full scope of nucleic acids with 90% identity to SEQ ID NO:1, 3 or 5.

Nucleic acids encoding proteins with 90% identity to the 682 amino acid long SEQ ID NO:2 would encode proteins with 68 amino acid substitutions relative to SEQ ID NO:2. Similarly, nucleic acids encoding proteins with 90% identity to 671 amino acid long SEQ ID NO:4 would encode proteins with 67 amino acid substitutions, and nucleic acids encoding proteins with 90% identity to 661 amino acid long SEQ ID NO:6 would encode proteins with 66 amino acid substitutions.

Nucleic acids with 90% identity to a 2049 nucleotide long nucleic acid like that of SEQ ID NO:1 would have 204 nucleotide substitutions, and thus encompass those that encode proteins with 204 amino acid substitutions relative to SEQ ID NO:2; these proteins would have

70% identity to SEQ ID NO:2. Similarly, nucleic acids with 90% identity to a 2016 nucleotide long nucleic acid like that of SEQ ID NO:3 would have 201 nucleotide substitutions, thus encompassing those that encode proteins with 201 amino acid substitutions, and nucleic acids with 90% identity to a 1986 nucleotide long nucleic acid like that of SEQ ID NO:5 would have 198 nucleotide substitutions, thus encompassing those that encode proteins with 198 amino acid substitutions.

Thus, the claims are drawn to nucleic acid that encode proteins with up to 204 amino acid substitutions relative to SEQ ID NO:2.

The instant specification fails to provide sufficient guidance for which amino acids of SEQ ID NO:2 can be altered and to which other amino acids, and which amino acids must not be changed, to maintain the activity of the encoded protein. The specification also fails to provide guidance for which amino acids can be deleted and which regions of the protein can tolerate insertions and still produce a functional protein.

The guidance in the specification with respect to making amino acids substitutions in AXMI-009 is as follows:

The specification, in the paragraph starting on pg 13, line 3, says:

> Amino acid substitutions may be made in nonconserved regions that retain function. In general, such substitutions would not be made for conserved amino acid residues, or for amino acid residues residing within a conserved motif, where such residues are essential for protein activity. Examples of residues that are conserved and that may be essential for protein activity include, for example, residues that are identical between all proteins contained in the alignment of Figures 1A, B, and C. Examples of residues that are conserved but that may allow conservative amino acid substitutions and still retain activity include, for example, residues that have only conservative substitutions between all proteins contained in the alignment of Figures 1A, B, and C. However, one of skill in the art would understand that functional variants may have minor conserved or nonconserved alterations in the conserved residues.

Conservative substitutions are defined on pg 12, lines 15-21. A search of the originally filed Fig. 1, shows that there are 2 positions that are identical among all the proteins in the

Figure, and 8 positions that have only conservative substitutions among all proteins.

The specification on pg 12, lines 9-13 suggests that substitutions be made at amino acids that are not essential for biological activity, but does not teach any such amino acids.

The specification teaches the 5 highly conserved regions among endotoxins in AXMI-009 (specification pg 4, lines 6-12); the regions encompass a total of 130 amino acids.

Thus, from the guidance in the specification, it would appear that the majority of the amino acids in SEQ ID NO:2, 4 and 6 could be substituted.

However, although point mutations and substitutions of a few amino acids have been made in Cry proteins, no one has substituted up to 204 amino acids of a Cry protein, as encompassed the claimed nucleic acids.

Making amino acid substitutions in *cry* proteins is unpredictable. Each *cry* protein only has activity against one or few insect species (de Maagd et al, 1999, Appl. Environ. Microbiol. 65:4369-4374, see pg 4369, column 1, paragraph 1), and even conservative substitutions in nonconserved regions can have unexpected effects on protein function (Figs 2 and 3). Even a single amino acid substitution in a *cry* protein may alter its insecticidal specificity, and toxicity must be determined empirically (Tounsi et al, 2003, J. Appl. Microbiol. 95:23-28; see pg 27, column 2, paragraph 2).

Aaronson et al (2001, FEMS Microbiol. Lett. 195:1-8) teach that there are extensive functional interactions between the three domains of Cry proteins and that more than one domain is involved in toxin specificity and binding (paragraph spanning the columns on pg 7). de Maagd et al (2001, Trends Genet. 17:193-199) teach that domains II and III are involved in insect specificity (pg 194, right column, paragraph 3) and that domains I and II have coevolved

towards certain specificities (pg 196, left column, paragraph 2, and pg 197, left column, paragraph 4). De Maagd et al (2001) concludes that the determination of insect specificity of endotoxins is still not understood (pg 198, right column, paragraph 2).

Thus, extensive teachings are required for making nucleic acids encoding *Cry* proteins with up to 204 amino acid substitutions relative to SEQ ID NO:2, as encompassed by the claimed nucleic acids. These teachings are not provided for by the specification. The specification also fails to overcome the unpredictability of making large numbers of amino acid substitutions in *Cry* proteins by providing no working examples of proteins with up to 204 amino acid substitutions relative to AXMI-009.

The specification also suggests making the claimed nucleic acids by random mutagenesis (pg 13, lines 14-19. However, Guo et al (2004, Proc. Natl. Acad. Sci. USA 101: 9205-9210) teach that while proteins are fairly tolerant to mutations resulting in single amino acid changes, increasing the number of substitutions additively increases the probability that the protein will be inactivated (pg 9209, right column, paragraph 2). Thus, making and analyzing proteins that have up to 204 random amino acid substitutions to find those that have pesticidal activity would require undue experimentation.

Thus, given the unpredictability making in amino acid substitutions in *cry* proteins, proteins with up to 204 amino acid substitutions relative to SEQ ID NO:2 would likely have a very different insect toxicity than AXMI-009, if such toxins could even be made.

As the specification does not describe the transformation of any plant with a pesticidal protein with 90% identity to SEQ ID NO:2, 4 or 6, nucleic acids with 90% identity to SEQ ID NO:1, 3 or 5, undue trial and error experimentation would be required to screen through the

myriad of nucleic acids encompassed by the claims and plants transformed therewith, to identify those with insect resistance, if such plants are even obtainable.

Given the claim breath, unpredictability in the art, undue experimentation, and lack of guidance in the specification as discussed above, the instant invention is not enabled throughout the full scope of the claims.

Applicant urges that in *Kubin*, nucleic acids encoding proteins with 80% identity to a sequence identifier were considered enabled in view of the *Wands* factors; the instant claims are drawn to nucleic acids with 90% or 95% identity and as in *Kubin*, the specification teaches show to make variants and calculate the percent identity and assay for activity (response pg 7-8).

This is not found persuasive because nucleic acids with 90% identity to SEQ ID NO:1 encompass those that encode proteins with 70% identity to SEQ ID NO:2, i.e., that have 204 amino acid substitutions in SEQ ID NO:2. The art indicates that even though much is known about Cry protein structure, not enough is known about the structure/function relationship to predict a protein's toxicity. The specification does not teach how to make these proteins.

Applicant urges that the structure of Cry proteins is known in the art, citing Li et al and Morse et al; these references provide guidance for determining the regions of a Cry protein that would tolerate modification and on which regions are involved in coleopteran activity for Cry3A (response pg 8).

This is not found persuasive. Applicant has not pointed to what parts of Li et al teach which regions are involved in coleopteran activity for Cry3A, and thus for SEQ ID NO:2. A teaching for the basic structure of Cry endotoxins does not teach which amino acids are involved

in coleopteran, lepidopteran and heteropteran pesticidal activity.

Applicant urges that Li teaches that the specificity determining regions of lepidopteran toxins Cry2A and Cry2B can be mapped by alignment to Cry3A structure; these proteins have similar identities to Cry 3A that the instant proteins do (response pg 8-9).

This is not found persuasive because deMaagd et al, 2001, teach that the determinants of insect specificity in Cry endotoxins is not understood (pg 198, right column, paragraph 2). Further, none of these references teach the determinants of heteropteran pesticidal activity.

Applicant urges that Rajamohan et al and Lee et al each which domain II residues are important for lepidopteran activity (response pg 9).

This is not found persuasive because de Maagd et al (2001, Trends Genet. 17:193-199) teach that domains II and III are involved in insect specificity (pg 194, right column, paragraph 3) and that domains I and II have coevolved towards certain specificities (pg 196, left column, paragraph 2, and pg 197, left column, paragraph 4). Thus, Rajamohan et al and Lee et al's teachings on domain II are not sufficient.

4. Claims 1-11, 19 and 22-26 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The rejection is repeated for the reasons of record as set forth in the Office action mailed 20 May 2008, as applied to claims 1-11, 19 and 22-23. Applicant's arguments filed 31 July 2008

have been fully considered but they are not persuasive.

The claims all require nucleic acids encoding a pesticidal protein with 90% or 95% identity to SEQ ID NO:2, 4 or 6 and nucleic acids with 90% or 95% identity to SEQ ID NO:1, 3 or 5, wherein the nucleic acid encodes a pesticidal protein. As nucleic acids encoding proteins with 90% identity to SEQ ID NO:2, 4 or 6 would encode proteins with up to 68 amino acid substitutions and nucleic acids with 90% identity to SEQ ID NO:1 encompass those that encode proteins with 204 amino acid substitutions relative to SEQ ID NO:2, the claims are drawn to a broad genus of nucleic acids.

The specification describes the 5 highly conserved regions among most Cry endotoxins; in the 682 amino acid long SEQ ID NO:2, the regions encompass a total of 130 amino acids (specification pg 4, lines 6-12).

The specification describes no relevant characteristics or motifs responsible for coleopteran, lepidopteran and heteropteran pesticidal activity.

Aaronson et al (2001, FEMS Microbiol. Lett. 195:1-8) teach that there are extensive functional interactions between the three domains of Cry proteins and that more than one domain is involved in toxin specificity and binding (paragraph spanning the columns on pg 7). de Maagd et al (2001, Trends Genet. 17:193-199) teach that domains II and III are involved in insect specificity (pg 194, right column, paragraph 3) and that domains I and II have coevolved towards certain specificities (pg 196, left column, paragraph 2, and pg 197, left column, paragraph 4). de Maagd et al (2001) concludes that the determination of insect specificity of endotoxins is still not understood (pg 198, right column, paragraph 2). Further, each *cry* protein only has activity against one or few insect species (de Maagd et al, 1999, Appl. Environ.

Microbiol. 65:4369-4374, see pg 4369, column 1, paragraph 1)

The specification does not describe the structure required for the recited function, nor does it describe the structural features that distinguish pesticidal protein-encoding nucleic acids with 90% identity to SEQ ID NO:1, 3 or 5 from other nucleic acids with 90% identity to SEQ ID NO:1, 3 or 5 or pesticidal proteins with 90% identity to SEQ ID NO:2, 4 or 6 from other proteins with 90% identity to SEQ ID NO:2, 4 or 6.

The only species reduced to practice in the specification is SEQ ID NO:1, 3 or 5, which encodes SEQ ID NO:2, 4 or 6. Since the disclosure fails to describe the common attributes that identify members of the genus, and because the genus is highly variant, SEQ ID NO:1, 3 or 5 alone is insufficient to describe the claimed genus.

Hence, Applicant has not, in fact, described nucleic acids encoding a pesticidal protein with 90% identity to SEQ ID NO:2, 4 or 6 and nucleic acids with 90% or 95% identity to SEQ ID NO:1, 3 or 5, wherein the nucleic acid encodes a pesticidal protein, within the full scope of the claims, and the specification fails to provide an adequate written description of the claimed invention.

Therefore, given the lack of written description in the specification with regard to the structural and functional characteristics of the claimed compositions, it is not clear that Applicant was in possession of the claimed genus at the time this application was filed.

Applicant urges that the instant claims meet the requirements for written description set forth by the Federal Circuit; a given sequence identity is recited, methods for determining the percent identity are known, variants are disclosed, numerous Cry sequences were known in the

art, and much was known about Cry protein structure (response pg 10-11).

This is not found persuasive because the structures associated with the claimed function, toxicity toward the Coleopterans Lepidopterans, and Heteropterans, are not known in the art or described in the specification. Comparison to the sequences in Fig 1 would not provide information of the structures required for that function, as cry 1Aa, cry 1Ac, crylCa and crylla are only toxic to Lepidopterans; cry3Aa, cry3Ba, cry3Bb, cry7Aa, and cry8Aa are only toxic towards Coleopterans; and cry4Aa, cry l 0Aa, cry l 6Aa, cry l9Ba, cry24Aa and cry40Aal are toxic only to mosquitoes, which are Dipterans, and are not plant pests. A comparison of these with SEQ ID NO:2 provides no indication of the protein structures responsible for SEQ ID NO:2 biological activity.

Applicant urges that it was known that Cry proteins have three domains, a helix bundle, a three-sheet domain and a beta sandwich motif, citing Li, providing very specific and define structural parameters to the claimed sequences; four of these domains are in the instant sequence and other teachings in the art describe domain II residues important for toxicity (response pg 11).

This is not found persuasive. These general characteristics are true of every Cry protein, including those with toxicity to lepidopterans, coleopterans, nematodes and mosquitoes and those native proteins that do not appear to have any toxicity at all (*e.g.*, cry25Aa). These basic structures are merely characteristics of Cry proteins. They are not specifically associated with the disclosed function, *D. virgifera virgifera*, *D. undecimpunctata*, *T. ni*, and *L. lineolaris* toxicity. de Maagd et al (2001, Trends Genet. 17:193-199) teach that domains II and III are involved in insect specificity (pg 194, right column, paragraph 3) and that domains I and II have coevolved towards certain specificities (pg 196, left column, paragraph 2, and pg 197, left

column, paragraph 4). de Maagd et al, 1999, teach that that the crystal structure of Cry1C only allows for limited prediction of the exact structure of Cry1Aa (pg 4373, right column, paragraph 4); thus, Li's teaching is insufficient for describing the structure/function relationship of the claimed nucleic acids. More than the Crystal structure and conserved regions are required for Cry protein function. Additionally, it is noted that the claims are not limited to nucleic acids encoding Cry proteins.

Applicant urges individual support for each species is not required; they have provided exemplary nucleotide and amino acid sequences and variants and fragments thereof, and numerous Cry proteins were known in the art, allowing one to envision that claimed invention (response pg 11-12).

This is not found persuasive because those of skill in the art say that the relationship between structure and function is not well-known in Cry proteins. Aaronson et al, de Maagd et al, 1999, and de Maagd et al, 2001, make it clear that the correlation between that function and a structure is not sufficiently known in cry proteins as a whole, and the specification does not describe the motifs and amino acids required for SEQ ID NO:2 biological activity. The specification does not make up for this deficit.

Applicant urges that the recitation of a predictable structure is sufficient to satisfy the written description requirement (response pg 12).

This is not found persuasive because that is only true if no functional limitations are in the claim. The functional limitation of coleopteran, lepidopteran and heteropteran pesticidal activity requires a description of the structure that confer that activity.

Applicant urges the claims recite functional characteristics that distinguish the claimed

sequences, as well as fragments (response pg 12-13).

This is not found persuasive. The recitation of the function does not describe the structures responsible for it. The relationship between structure and the specific pesticidal function was not described in the specification. SEQ ID NO:3 and 5, which encode 671 and 661 amino acid long fragments, respectively, of the 682 amino acid long SEQ ID NO:2 do not describe proteins with 203 amino acid substitutions relative to SEQ ID NO:2.

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 1-11, 19 and 22-26 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter that Applicant regards as the invention. Dependent claims are included in all rejections.

Claims 1, 19 and 22-26 are indefinite in their recitation of "coleopteran, lepidopteran and heteropteran activity". As "coleopteran, lepidopteran and heteropteran" refer to insect families, and not to a type of activity, it is unclear what the phrase means. If Applicant means that the protein has pesticidal activity towards coleopterans, lepidopterans and heteropterans, the claims should be so amended.

Claim Rejections - 35 USC § 103

7. The following is a quotation of 35 U.S.C. 103(a), which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are

such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

8. Claims 1, 4-7 and 24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ben-Dov et al (1996, Appl. Environ. Microbiol., 62:3140-3145) in view of Carlton et al (1985, Mol. Biol. Microb. Differ., Proc. Intl. Spore Conf., 9th, Meeting date 1984, pages 246-252; Ed. Hoch et al, Am.Soc. Microbiol., Washington, DC) and taken with the evidence of Applicant's response to the Request for Information under 37 CFR 1.105.

Applicant's response to the Request for Information under 37 CFR 1.105, filed 17 March 2009, indicate that the bacterial strain from which SEQ ID NO:1-6 were isolated is HD536, and available from the USDA.

The claims are drawn to a nucleic acid encoding a toxin comprising SEQ ID NO:2, 4 or 6.

Ben-Dov et al teach cloning of delta-endotoxin genes from a *Bacillus thuringiensis* plasmid (pg 3141. left column, to pg 3143, right column, paragraph 3). The genes were cloned in vectors that encode a selectable-marker protein heterologous to the endotoxin, and these clones were grown in an E. coli host cell (pg 3140, right column, paragraph 2). Ben-Dov et al do not teach a nucleic acid encoding a SEQ ID NO:2, 4 or 6.

Carlton et al teach that strain HD536 has a 68 MDa plasmid implicated in toxin production (Table 1).

At the time the invention was made, it would have been obvious to one of ordinary skill in the art to modify the method of cloning delta-endotoxin genes from *B. thuringiensis* plasmids as taught by Ben-Dov et al, to clone delta-endotoxin genes from strain HD536 described in Carlton et al. One of ordinary skill in the art would have been motivated to do so because an increased repertoire of delta-endotoxins would be desirable for increasing toxicity spectra and for

overcoming pest resistance to existing endotoxins. It is obvious to use the 68 MDa plasmid from HD536 because HD536 was known in the art as having a toxin-encoding plasmid (Carlton et al, Table 1). In cloning the toxins from the 68 MDa plasmid from HD536 one of skill in the art would necessarily isolate a nucleic acid encoding SEQ ID NO:2, 4 or 6. It would be obvious to one of skill in the art to culture the host cell comprising the plasmid in conditions under which the nucleic acid encoding the toxins is expressed to study the toxicity of the protein, particularly for toxicity to coleopteran, heteropteran or lepidopteran plant pests.

9. Claims 2-3, 8-11, 19, 22-23 and 25-26 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ben-Dov et al in view of Carlton et al as applied to claims 1, 4-7 and 24 above, and further in view of Koziel et al (1997, US Patent 5,625,136).

The claims are drawn to plants transformed with a nucleic acid encoding a toxin comprising SEQ ID NO:2, 4 or 6, including plant optimized nucleic acids.

The teachings of Ben-Dov et al in view of Carlton et al are discussed above. Ben-Dov et al in view of Carlton et al do not teach plants and seeds transformed with the nucleic acid.

Koziel et al teach construction of a Cry endotoxin coding sequence that is designed for expression in a plant; this sequence has increased GC content relative to the native coding sequence (column 7, lines 19-56; column 9, lines 50-56). Koziel et al also teach expression of the modified Cry endotoxin coding sequence in maize cells from a victor that also encodes phosphoenolpyrivate carboxylase (column 59, line 40, to column 63, line 50), as well as maize plants and seeds transformed with the modified Cry endotoxin coding sequence (claims 4-25).

At the time the invention was made, it would have been obvious to one of ordinary skill in the art to transform the nucleic acid taught by Ben-Dov et al in view of Carlton et al into

plants, including maize, as described in Koziel et al. One of ordinary skill in the art would have been motivated to do so because the resultant plants will be more resistant to insect pests, and the farmer thus less likely to suffer economic loss because of them.

Conclusion

10. No claim is allowed.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anne R. Kubelik, whose telephone number is (571) 272-0801. The examiner can normally be reached Monday through Friday, 8:30 am - 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anne Marie Grunberg, can be reached at (571) 272-0975.

The central fax number for official correspondence is (571) 273-8300.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

Anne Kubelik, Ph.D.
July 15, 2009

/Anne R. Kubelik/
Primary Examiner, Art Unit 1638